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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,244	06/27/2001	Barry S. Fogel	0264724-0031	4907

24280 7590 02/24/2005

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EXAMINER	
WILLIAMS, LEONARD M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/893,244	FOGEL, BARRY S.	
	Examiner	Art Unit	
	Leonard M Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-88* is/are pending in the application.

4a) Of the above claim(s) *1-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *81-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Examiner notes receipt of the Response to Restriction/Election Requirement received on August 25, 2004. The applicant elects Group II claims 81-88 without traverse. The examiner is withdrawing the species election requirement set forth in the office action of July 7, 2004. The restriction/election requirement is made final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 81-84 are rejected under 35 U.S.C. 1 12, first paragraph, because the specification, while being enabling for compounds enhancing GABA-A neurotransmission (acamprosate) and for compounds capable of decreasing NMDA-type glutamate neurotransmission (magnesium N-acetylhomotaurinate, memantine, magnesium sulfate, magnesium oxide), does not reasonably provide enablement for "A composition comprising at least two agents...". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the ad; (4) the predictability or unpredictability of the ad; (5) the breadth of the claims', (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention:

The rejected claims are drawn to "A composition comprising at least two agents, the composition having activities of: (i) enhancing GABA-A neurotransmission (ii) decreasing NMDA-type glutamate neurotransmission".

(2) Breadth of the Claims:

The breadth of the claims are exceptionally broad encompassing any compositions comprising at least two agents. The phrase "...having activities of..." with subsequent description of the activities desired are intended use descriptors of "A composition comprising at least two agents..." and thus are not given patentable weight as being part of the preamble. A preamble is generally not accorded any patentable

weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

(3) Guidance of the Specification:

The guidance of the specification as to "a composition comprising at least two agents" is limited to agents having GABA-agonist activity and/or NMDA antagonist activity. With specific examples being acamprosate, magnesium N-acetylhomotaurinate, memantine, magnesium sulfate, and magnesium oxide.

Compounds possessing other activities are not described in an enabling fashion.

(4) Working Examples:

The applicant provides working examples in case reports 1-6 including including various compositions containing acamprosate, memantine, magnesium oxide, and magnesium chelates either singularly or in conjunction with each other as being effective in the treatment of tardive dyskinesia.

(5) State/predictability of the Art:

The state of the art regarding the testing of all compositions comprising at least two agents to determine if they have GABA-A agonist and or NMDA antagonist activity is high.

(6) The Quantity of Experimentation Necessary:

The instant claims read on any composition having at least two agents. As discussed above, the specification fails to provide sufficient support for agents other than those having GABA-agonist activity and/or NMDA antagonist activity. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation (i.e. experimenting with all compositions having at least two agents). Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Accordingly the claims are evaluated as being drawn to a composition comprising at least two agents where the first agent has GABA agonist activity (enhancing GABA-A neurotransmission) and the second agent has NMDA antagonist activity (decreasing NMDA-type glutamate neurotransmission).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 82 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition

so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "compound" in claim 82 is used by the claim to mean "a composition comprising at least two agents", while the accepted meaning is "a single agent." The term is indefinite because the specification does not clearly redefine the term.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 81-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Olney (US Patent No. 5474990).

Olney teaches, in col. 11 line 60 to col. 12 line 35, that barbiturates acting as direct agonists to GABA receptors can be used as "safening agents" to prevent the neurotoxic effects caused by the use of NMDA antagonists.

Olney teaches, in col. 16 line 60 to col. 17 line 6, a composition of matter comprising a mixture of an NMDA antagonist and a barbiturate, wherein the NMDA antagonist is present in a dosage that can protect the central nervous system against excitotoxic damage, and wherein the barbiturate acts as a direct GABA agonist anticipating the "...composition comprising at least two agents...(i) enhancing GABA-A

neurotransmission (ii) decreasing NMDA-type glutamate neurotransmission" of claim 81, the "...composition...is a compound" of claim 82, and the "...composition...is a mixture" of claim 83.

Olney teaches, in example 1, that the NMDA antagonist can be MK-801 (a NMDA selective antagonist) and that the GABA-agonist specific barbiturates can be pentobarbital, secobarbital or thiamylal anticipating the "...composition...wherein neither agent has both activities" of claim 84.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 85-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Durlach (US Patent No. 4355043), and further in view of Primes et al. (US Patent No. 4582705).

Durlach teaches, in examples 1-6, the synthesis of a variety of N-acetylaminopropanesulfonic acid salts including sodium (example 1), potassium (example 2), lithium (example 3), calcium (example 4), magnesium (example 5) and zinc (example 6). Acamprosate is calcium-N-acetylaminopropane sulfonate (example 4). Durlach teaches, in col. 4 line 10 to col. 6 line 30, that the various N-acetylaminopropanesulfonic acid salts can be used anti-convulsants, neurotropic agents (calcium salt), vasculotropic agents (magnesium salt), antiasthenic agents (potassium salt), and for bipolar disorder treatment (lithium salt).

Durlach does not teach acamprosate in combination with an inorganic salt or a a chelate of magnesium (except for magnesium-N-acetylaminopropanesulfonate).

Primes et al. teach, in col. 1 line 10 to col. 2 line 60, compositions and methods for the detoxification of alcoholics including a standard treatment protocol of 1) drug therapy, 2) nutritional therapy and 3) psychotherapy. The drug therapy includes administration of thiamine hydrochloride (100-300 mg), pentobarbital sodium (a GABA-agonist barbiturate, 100-200 mg), diphenylhydantoin sodium (100-200 mg) and dextro-amphetamine (5-50 mg). The nutritional therapy includes a high caloric diet supplemented by vitamins. Magnesium replacement therapy is proposed, specifically magnesium sulfate therapy (2g) for treatment of the seizures and fevers that accompany alcohol withdrawl. Prime et al. teach in, col. 3 lines 5-30, that large quantities of magnesium salts may be needed in the detoxification of alcoholics (5-50 g) with the magnesium salts being selected from magnesium chloride, magnesium sulfate, or magnesium citrate.

On page 17 of the applicants specification it states: "Acamprosate (calcium N-acetylhomotaurinate) is the calcium salt of homotaurine, a derivative of the amino acid taurine. It is used clinically in the treatment of abstinent alcoholics to reduce or inhibit their craving for alcohol. Acamprosate, which is chemically similar to the inhibitory neurotransmitter GABA, is a GABA agonist, particularly at GABA-A receptors." It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Durlach's calcium-N-acetylaminopropanesulfonate compound (acamprosate) in conjunction with a magnesium salt (specifically magnesium sulfate), as Prime et al. demonstrated that magnesium sulfate has benefit in the treatment of alcoholics. Prime et al. also disclose that pentobarbital sodium, a GABA-agonist barbiturate, is used in the drug therapy aspect of detoxifying alcoholics. It would have been obvious to one of ordinary skill in the art at the time the invention was made that any GABA-agonist compound could be used in the drug therapy. One of ordinary skill in the art at the time the invention was made would have been motivated to use the calcium-N-acetylaminopropanesulfonate instead of pentobarbital sodium in the treatment of alcoholics as it has fewer sideeffects. One of ordinary skill in the art would have been motivated to try differing ratios of magnesium salts to acamprosate in order to modulate and maximize the effectiveness of the alcohol detoxification process, as too little or too much magnesium salt would have adverse consequences (non-effectiveness in alcohol detoxification or misadjustment of the electrolyte balance). One of ordinary skill in the art at the time the invention was made would expect a reasonable chance of success as

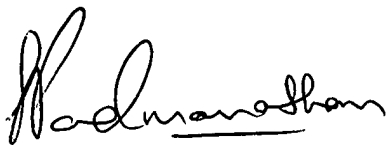
both compounds have been used separately to treat the same therapeutic target combining them should have increased benefit.

The examiner respectfully points out the following from MPEP 2144.06: "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re* Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

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LMW